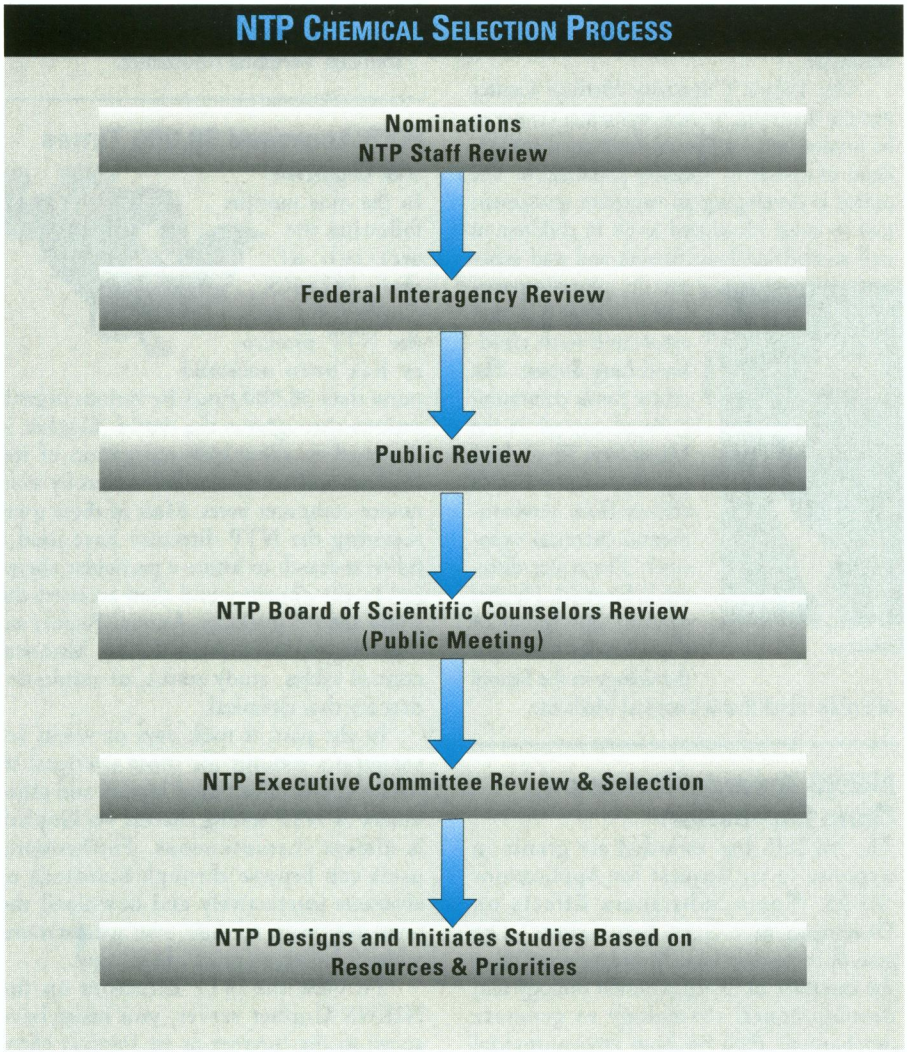
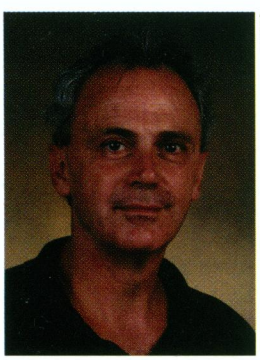


Orleans. McLachlan leaves the NIEHS after serving as scientific director longer than any of his predecessors, having developed and implemented many new initiatives including a major reorganization of the institute's intramural research program. During his tenure, the NIEHS established a clinical program in collaboration with UNC-CH and Duke University, and established education and outreach efforts including summer internships and an annual environmental career symposium for high school students and teachers. As scientific director, McLachlan supervised a workforce of approximately 700 scientists and support personnel in 19 different laboratories and branches and oversaw a yearly budget in excess of $90 million. McLachlan's hallmark was his emphasis on basic research while facilitating the application of fundamental findings to toxicology testing and human studies.

During McLachlan's early years at the institute, not everyone would have labeled him as potential executive material, despite his high energy and incisive intellect. He has often joked about his inclination to wear sandals and other "hippie" attire. However, he amply demonstrated his abilities with his scientific successes and solid leadership as head of the developmental endocrinology and pharmacology section, in the Laboratory of Reproductive and Developmental Toxicology beginning in 1976. He later became the laboratory chief, a post he retains until his departure for Tulane.


NIEHS

John A. McLachlan

McLachlan is internationally known for his research on diethylstilbestrol (DES) and the health effects of other environmental estrogens. He was one of the first to recognize the global health implications of environmental estrogens both in terms of research and policy. Using a mouse model, he confirmed the association between maternal use of DES and cancers and malformations of the female reproductive tract in offspring and further identified malformations in male offspring as well. His recent findings on the ontogeny of the estrogen response and the role of growth factors and related signaling pathways in estrogen action continue to provide provocative new ideas for biology and medicine. Since 1979, he has been at the center of organizing several international conferences on estrogens in the environment. McLachlan has delivered over 120 invited lectures and published more than 150 research and overview articles in the scientific literature.

In a memo to NIEHS employees announcing his decision, McLachlan said, "Like many of you, I have spent most of my adult life at the institute and regard it, and you, with utmost respect and affection. It will be hard to go, but new opportunities and challenges afforded at Tulane excite and energize me." NIEHS Director Kenneth Olden called McLachlan a leader in his field and said he plans to have him back to NIEHS as a visiting scientist. "John will continue to be a part of the institute," Olden said. The search for a new scientific director is in progress.

NTP Invites Chemical Nominations

The National Toxicology Program invites members of the public, unions, industry groups, state and local governments, environmental organizations, academia, etc., to nominate chemicals or other agents to be studied by the NTP.

Of the 70,000 substances in commerce, adequate toxicological data are available for only 10–20%. Identifying those chemicals that have the potential to produce an adverse health effect has been the primary objective of the NTP. Established in 1978, the NTP coordinates toxicology studies within the Department of Health and Human Services. NTP's member agencies are NIH's National Institute of Environmental Health Sciences, FDA's National Center for Toxicological Research, and CDC's National Institute for Occupational Safety and Health.

Including studies done under its predecessor, the NCI Cancer Bioassay Program, NTP has completed more than 400 two-year studies in rats and mice since its establishment. Technical reports have been published for each of these bioassays, and most are available as bound booklets through the NTP Data Management Group, [telephone (919) 541-3419] or through the National Technical Information Service in Springfield, Virginia. Traditional toxicity tests, such as the two-year chronic bioassay to detect carcinogens, have been the basis for most regulatory

decisions regarding the safety of environmental chemicals. Testing the high priority chemicals is critical to achieving the overall NTP goal of protecting public health by preventing exposures and generating the data that can make risk assessments more reliable. Abstracts of NTP study results and other NTP data and information are also available through the Internet, a relatively recent development which has greatly expanded dissemination of NTP information (see adjoining story).

There are no restrictions on chemical nominations; they may focus on individual chemicals, classes of chemicals, or broad public health issues. Nominations may be made for studies that will 1) identify chemical hazards, 2) improve the risk assessment process, 3) test hypotheses of mechanisms of action, 4) reduce the number of animals needed for toxicity/carcinogenicity evaluations, or 5) lead to new mechanistically based short-term tests.

The more information presented in a chemical nomination, the stronger the nomination. It is essential that specific and substantive reasons why a chemical should be studied are given. If possible, the nomination should contain the Chemical Abstracts Service (CAS) number of the chemical, especially if it has more than one name. CAS numbers can be obtained from *The Merck Index,* available in the reference sections of most public and university libraries. Information on the volume of chemical manufactured or in use and information on its uses is also helpful. A bibliography of any previous research is valuable, including animal and other laboratory studies, epidemiological studies, and medical case studies.

However, even if little or none of this background information is available, nominations will still be considered. Every letter of nomination will receive a response. Letters nominating chemicals and supporting information should be sent to:

Chemical Nomination Office c/o Errol Zeiger MD A2-02, NIEHS, PO Box 12233, Research Triangle Park, NC 27709 USA.

Nomination Principles for NTP Studies

The NTP Executive Committee operates under the principle that industry will evaluate chemicals or other agents for health and environmental effects as intended and mandated by the Congress under legislative authorities. The NTP, acting under its nomination principles, will solicit nominations for NTP studies from the following categories:

1. Chemicals found in the environment that are not closely associated with a single commercial organization;
2. Biological or physical agents that may not be adequately evaluated without federal involvement;
3. Commercial chemicals with significant exposure that were first marketed before current testing requirements or those that generate too little revenue to support further evaluations;
4. Potential substitutes for existing chemicals or drugs that might not be developed without federal involvement;
5. Substances that occur as mixtures for which evaluations cannot be required of industry;
6. Chemicals or agents that will aid our understanding of chemical toxicities, or our understanding of the use of test systems to evaluate potential toxicities;
7. Chemicals that should be evaluated to improve the scientific understanding of structure–activity relationships and thereby help limit the number of chemicals requiring extensive evaluations;
8. Emergencies or other events that warrant immediate government evaluation of a chemical or agent.

The NTP will assess the specific needs for studies, evaluate existing literature and testing data, assess ongoing evaluations in the government and private sector, and also determine how the chemical fits into an overall plan for improving the test systems before committing to specific studies. The selection of a chemical or agent by the NTP Executive Committee does not automatically commit the NTP to evaluate that chemical or agent. The priority of the chemicals and the proposed studies are assessed during the selection of contractors to conduct the studies. During any of these phases the chemical or study may be withdrawn if higher priority studies are found, or if the study proves to be impractical.

NTP to Study 22 Chemicals

The following chemicals are being considered for short- and long-term toxicology and carcinogenesis studies. The NTP welcomes comments on these chemicals and relevant information including ongoing toxicological studies, current or future trends in production and import, use patterns, human exposure levels, environmental occurrence, and toxicological data.

Contact may be made by mail to: William Eastin, NIEHS/NTP, PO Box 12233, Research Triangle Park, NC 27709, by telephone (919) 541-7941, FAX (919) 541-4714, or E-mail at Eastin@NIEHS. NIH.GOV.

Riddelliine (CAS no. 23246-96-0). Two-year studies via oral gavage in B6C3F$_1$ mice and F344 rats. Riddelliine is a pyrrolizidine alkaloid found in plants of the genus *Senecio* in the western United States. Riddelliine and other alkaloids in these plants can cause the death of livestock if ingested in high quantities, or may contaminate meat as a residue. Riddelliine may also contaminate commercial grains, milk, and honey, and is found in some herbal teas. In NTP 90-day studies riddelliine was found to cause hepatic toxicity in mice and rats and hepatic neoplasia in rats. Two-year carcinogenicity studies of standard design are proposed to determine the shape of the dose–response curve for carcinogenicity in rats, and further evaluate the toxic and carcinogenic potential in mice.

Urethane/ethanol mixture (CAS no. 51-79-6/64-17-5). Two-year studies via dosed-water in B6C3F$_1$ mice and F344 rats. Urethane and ethanol are byproducts of fermentation and are commonly found in alcoholic beverages and in many foods. Urethane has been recognized as a rodent and nonhuman primate carcinogen, while the International Agency for Research on Cancer has determined that alcoholic beverages are human carcinogens. Two-year studies that are planned will include separate groups of male and female mice exposed to urethane (CAS no. 51-79-6), ethanol (CAS no. 64-17-5), or to several levels of urethane and ethanol in the drinking water. The studies will include an assessment of the toxicokinetics of urethane, with and without ethanol, following repeated dosing. Studies of urethane DNA adducts are planned to address the issue of the dosimetry of DNA alterations.

Dichlorodiphenyl sulfone (CAS No. 80-07-9). Two-year studies via dosed-feed in B6C3F$_1$ mice and F344 rats. Dichlorodiphenyl sulfone is a component of high temperature plastics. A known inducer of cytochrome P450s, dichlorodiphenyl sulfone was shown to cause marked hepatomegaly in NTP prechronic studies. Other studies have shown facile oral absorption and a relatively simple metabolite pattern, as well as self induction of metabolism with repeated administration. Carcinogenicity studies with dichlorodiphenyl sulfone are planned with both sexes of rats and mice.

Elmiron (CAS no. 37319-17-8). Fourteen-day studies via oral gavage in B6C3F$_1$